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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,060	WILD ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7 and 30-40* is/are pending in the application.

4a) Of the above claim(s) *35-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7 and 30-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Previously, the Applicant elected with traverse the inventions of Group I (immunogenic compositions comprising a viral envelope protein, a stabilizing peptide, and a viral cell surface receptor), and the species wherein the stabilizing peptide was SEQ ID NO: 1.

2. In the prior action, claims 1-8 and 30 were under consideration and rejected, and claims 9-29 were withdrawn as to non-elected inventions. In the Response of February 23, 2006, the Applicant amended claims 1, 7, and 30; cancelled claims 2-6, and 8-29; and added new claims 31-40.

In amending the claims, the Applicant has cancelled reference to the elected species of SEQ ID NO: 1. It is noted that such a cancellation is permitted after a species election under MPEP § 803.02. However, the Markush type practice described in MPEP § 803.02 applies only where the species meet the unity of invention test set forth in In re Harnisch, 206 USPQ 300 (CCPA 1980), which requires that the species within a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility.

In the present case, while the species of SEQ ID NO: 1 appears to share a fair amount of sequence homology to SEQ ID NOs: 2-4 and 9 (SEQ ID NO: 9 is a fragment of SEQ ID NO: 1), the same is not true regarding SEQ ID NOs: 5-7. Thus, while the cancellation of SEQ ID NO: 1 is permitted in view of the presence of SEQ ID NOs: 2-4 and 9 in the claims, the Markush type practice will not be extended to the species represented by SEQ ID NOs: 5-7.

3. The examination of the claims was extended to the peptide of SEQ ID NO: 2, which species is rejected for the reasons indicated below. In view of these rejections, claims 35-40, drawn to peptides other than SEQ ID NO: 2, are withdrawn from examination.

4. Currently, claims 1, 7, 30-34 are under consideration.

Specification

5. **(Prior Objection- Withdrawn)** The specification was objected to for referring to protein or nucleic acid sequences without also identifying them by the sequence identifier assigned to them in the sequence listing as required by 37 CFR 1.821(d). See e.g., p. 23, line 6.In view of the amendment to the application to insert the appropriate sequence identification number, the objection is withdrawn.

6. **(Prior Objection- Withdrawn)** The disclosure was objected to because of the following informalities: the application referred on page 63 to Figure 4B as showing reduction in viral replication in a conducted assay. In view of the amendment of the application such that it now refers to Figure 7B, the objection is withdrawn.

Claim Objections

7. **(Prior Objection- Withdrawn)** Claim 6 was objected to because of the following informalities: a comma should be inserted between the last two items in the list of alternatives provided in the claim. In view of the cancellation of the claim, the objection is withdrawn.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. **(Prior Rejection- Withdrawn)** Claims 1-8 and 30 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was not clear what the relationship was (structurally) between the viral envelope protein and the stabilizing peptide, or what is being referred to by the phrase "structural intermediates." In view of the amendments of the claims, and the teachings in the art and application indicating how the peptide of SEQ ID NO: 2 associates with the target viral envelope protein complex, the rejection is withdrawn.

10. **(Prior Rejection- Withdrawn)** Claims 1-5, 7, 8, and 30 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was not clear what was meant by the phrase "structural intermediate" in the claim. In view of the amendment of the claims limiting them to the envelope protein comprising the gp41/gp120 complex, and the teachings in the art and application indicating how the peptide of SEQ ID NO: 2 associates with the target viral envelope protein complex, the rejection is withdrawn.

11. **(Prior Rejection- Withdrawn)** Claims 1-6 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was unclear if the claim language indicating that the stabilizing peptide "is capable of associating" with the envelope protein required that the peptide and envelope protein were actually required to be associated in the claimed compositions. In view of the cancellation of claims 2-6, and the amendment of claim 1 to require that the peptide associates with the envelope protein, the rejection is withdrawn.

12. **(Prior Rejection- Withdrawn)** Claim 6 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. In view of the cancellation of the claim, the rejection is withdrawn.

13. **(New Rejection- Necessitated by Amendment)** Claims 1 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is treated as representative. This claim is drawn to a composition comprising "at least one viral envelope protein or fragment thereof... wherein said viral envelope protein of fragment thereof is the gp41/gp120 complex." By reference to "gp41/gp120 complex," and in view of the comments on (e.g.) page 16 and 17 indicating the claim language refers to "whole gp41," it appears that the Applicant intended to refer to the gp41/gp120 complex in its native configuration. This is because reference to the indicated complex implies the complex in its native form, and not fragments or variants thereof. This further supported by the Applicant's arguments indicating that the complex comprises at least the full-length gp41 protein.

However, the claims also describe the claimed composition has comprising any "viral envelope protein or fragment thereof." The claim further indicated that the "gp41/gp120 complex" represents a "viral envelope protein or fragment thereof." It is therefore unclear if the claims are intended to read on compositions comprising fragments of the indicated complex, or if, as indicated above, the claims are directed to complete forms of the gp41/gp120 complex. It is suggested that the "or fragments thereof" language be deleted from claim 1.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. **(Prior Rejection- Withdrawn)** Claims 1, 2, 4, 6-8, and 30 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement with respect to embodiments of the claimed inventions comprising any viral envelope protein, and any stabilizing peptide that is capable of disrupting the formation of one or more structural intermediates necessary for viral fusion and entry. Claims 2, 4, 6, and 8 have been cancelled from the application, and claims 1, 7, and 30 have been amended. In view of the amendments to the claims, the rejection is therefore withdrawn from these claims.

16. **(Prior Rejection- Maintained)** Claims 1-8 and 30 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims were rejected to extent that they read on embodiments of the claimed composition wherein the stabilizing peptides may be any stabilizing peptide, or may be any fragments, functional equivalents, homologues, or analogs of SEQ ID NO: 1 (the previously elected species). The claims have been amended to refer only to specific stabilizing peptides other than that of SEQ ID NO: 1, and to fragments thereof. The Applicant asserts that the amendments have overcome the rejection.

However, it is noted that in the statement of the rejection in the prior action, the claims were also rejected for inclusion of any fragment of the peptide of SEQ ID NO: 1- of which several of the indicated peptides are homologues. The peptide of SEQ ID NO: 2 is treated as

representative. The peptide of SEQ ID NO: 2 is identified in the Wild reference as a homologue of the DP-178 peptide- another name for the peptide of SEQ ID NO: 1. In the prior rejection, it was noted that Wild reference teaches that with very limited exceptions, the peptide was not amenable to deletions in its sequence. See e.g., PNAS 91:9770-74, at 9771-72 (teaching much reduced antiviral activity in DP-178 with truncations of up to 3 residues to N-terminus, no activity in peptides with C-terminal deletions). Thus, the art indicates that there is uncertainty in ability of any particular fragment of the indicated peptides to bind to the gp41/gp120 complexes. In view of this uncertainty, and the lack of any identification in the application of essential minimal regions of the these peptides for the required function, the claims were rejected for lack of sufficient descriptive support with respect to fragments of the indicated peptides.

The Applicant provided no response to these concerns except for the assertion that the claim amendments have overcome the rejection. As the amended claims still read on fragments of the identified peptides, the rejection is maintained for the reasons above and of record.

17. **(New Rejection- Necessitated by Amendment)** Claims 1, 7, and 30-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed compositions wherein the envelope protein is an human immunodeficiency virus (HIV) gp41/gp120 complex, does not reasonably provide enablement for the claimed compositions wherein the envelope protein is any gp41/gp120 complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors considered most relevant are the breadth of the claims, the presence of absence of working examples, and the nature of the invention.

Claims 1, 7, and 30 have been amended to require that the viral envelope protein is a gp41/gp120 complex, and that the stabilizing peptide is SEQ ID NO: 2. New claims 30-34, each dependent from one of claims 1, 7, or 30, have also been added to the application. With respect to the envelope proteins comprising the gp41/gp120 complex, it is noted that although the application refers to HIV gp41/gp120 complexes (page 1-2), the claims do not require that these proteins are HIV proteins. Nor is there any definition of the term "gp41/gp120 complex" in the application limiting the phrase to reference to the HIV derived complex. Further, it is known in the art that at least one other virus comprises a gp41/gp120 complex- the simian immunodeficiency virus. See e.g., Chen et al., Structure 13:197-211. Thus, the claims read on compositions comprising any gp41/gp120 complex and a stabilizing peptide as identified in the claims, wherein the peptides associate with the envelope protein.

The teachings of the present application provided in support of the claims were described in the prior action. The stabilizing peptides identified in the claims, of which SEQ ID NO: 2 is representative, are described in the application as peptides derived from the Human immunodeficiency virus (HIV). The teachings of the application provide examples demonstrating only that these peptides bind HIV envelope proteins. There is no demonstration that the indicated stabilizing peptides would be able to associate with envelope proteins of other viruses, including the SIV virus, so as to result in the claimed immunogenic composition.

The art does provide teachings relating to the nature of the identified peptides. In particular, the Wild reference (of record in the March 2001 IDS) indicates that certain of these peptides were known in the art as homologues to a stabilizing peptide known as DP-178. Wild et al., PNAS 91:9770-74, at page 9771 (Figure 1- showing homology between DP-178 and the peptide of SEQ ID NO: 2). In addition to disclosing the stabilizing peptide, the Wild reference also teaches that the inhibitory effect of the DP-178 peptide was HIV-1 specific. Page 9771, right column. The reference further teaches that the homologues of this peptide, including that of SEQ ID NO: 2, had similar characteristics to the DP-178 peptide. Page 9773, left column. Thus, the art indicates that, while the peptide of SEQ ID NO: 2 would be capable of associating with HIV envelope proteins, it would not be capable of associating with any gp41/gp120 envelope protein complexes.

In view of the teachings of the art regarding the nature of the stabilizing peptides identified in the claims, and the lack of any demonstration that these peptides would be capable of associating with gp41/gp120 complexes other than those from HIV, the claims are rejected for exceeding the scope for which the application provides an enabling disclosure.

Claim Rejections - 35 USC § 102

18. **(Prior Rejection- Withdrawn)** Claims 1, 2, and 6 were rejected under 35 U.S.C. 102(b) as being anticipated by Rimsky et al. (J Virol 72: 986-993). In view of the amendment of claim 1, and the cancellation of claims 2 and 6, the rejection is withdrawn.

19. **(Prior Rejection- Withdrawn)** Claims 1, 2, and 6 were rejected under 35 U.S.C. 102(b) as being anticipated by Kliger et al. (J Mol Biol 295: 163-68, of record in the May 2001 IDS). In view of the amendment of claim 1, and the cancellation of claims 2 and 6, the rejection is withdrawn.

20. **(Prior Rejection- Withdrawn)** Claims 1-5 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Wild et al. (WO 94/02505- of record in the May 2001 IDS). In view of the amendment of claim 1, and the cancellation of claims 2 –5 and 8, the rejection is withdrawn.

21. **(Prior Rejection- Withdrawn)** Claims 1-6 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Bolognesi et al. (WO 94/28920- of record in the May 2001 IDS). In view of the amendment of claim 1, and the cancellation of claims 2 and 6, the rejection is withdrawn.

22. **(Prior Rejection- Withdrawn)** Claims 1-8 and 30 were rejected under 35 U.S.C. 102(b) as being anticipated by Furata et al. (Nat Struct Biol 5: 276-79- of record in the May 2001 IDS). In view of the amendments to claims 1, 7, and 30, and the cancellation of claims 2-6 and 8, the rejection is withdrawn.

23. **(Prior Rejection- Withdrawn)** Claims 1, 2, and 6 were rejected under 35 U.S.C. 102(e) as being anticipated by Root et al. (U.S. 2001/0047080, which claims priority to U.S. provisional

application 60/171042). In view of the amendments to claim 1, and the cancellation of claims 2 and 6, and the arguments presented in traversal, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. **(New Rejection- Necessitated by Amendment)** Claims 1, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furata et al. (Nat Struct Biol 5: 276-79) in view of Wild et al., (PNAS 91:9770-74) (both references of record in the March 2001 IDS). Claim 1 was previously rejected over Furata. The claim has now been amended to exclude SEQ ID NO: 1 as the stabilizing peptide. Claim 31 further limits the claim to embodiments wherein the peptide is SEQ ID NO: 2.

The teachings of Furata were previously described. As indicated in the prior action, the reference teaches a composition comprising soluble CD4, and HIV gp41/gp120 complex, and the stabilizing peptide of SEQ ID NO: 1. However, the reference does not teach embodiments wherein the peptide is SEQ ID NO: 2.

However, Furata does teach that the use of the indicated method to determine the ability of DP178 to bind to an HIV envelope protein. See e.g., page 277 (description for Figure 1). It would therefore have been obvious to those in the art to use this method for the detection the ability of DP-178 homologues to also bind to HIV envelope proteins.

Wild teaches such homologues, including the homologues of the DP-178 peptide, including the peptide of SEQ ID NO: 2. See e.g., page 9771, Figure 1. Further, the reference also indicates that the ability of DP-178 to inhibit HIV infection varies with the HIV isolate targeted. See e.g., page 9772 (Table 1). From these teachings, it would have been obvious to those in the art to use the method of Furata to determine the ability of the homologue SEQ ID NO: 2 to bind to the envelope proteins of the different HIV isolates, with the result that the claimed compositions would be formed.

Those of ordinary skill in the art would have had a reasonable expectation of success in the combination based on the fact that the Furata reference demonstrated that the disclosed method was effect to detect peptide binding to HIV envelope proteins.

Thus, the combined teachings of the cited references render the claimed inventions obvious.

26. **(New Rejection-Necessitated by Amendment)** Claims 1, 7, and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furata in view of Wild as applied to claims 1 and 31 above, and further in view of Haddrick et al. (J Virol Methods 61:89-93). These claims read on compositions such as described by claims 1 and 31 above, except that these compositions require that the gp41/gp120 complex is part of a non-infectious viral particle.

The teachings of Furata and Wild have been described above. As was previously described, the Furata reference teaches the use of cells comprising an HIV envelope protein to determine the binding of stabilizing peptides to the protein. The reference does not teach the use of a non-infectious viral particle. However, from the teachings of the reference, it is apparent that

the purpose of the cells is merely as a carrier for the viral envelope proteins such that live HIV need not be used. Thus, it would have been obvious to those of ordinary skill in the art to use other such carriers of the viral envelope protein in the place of the cells.

Haddrick teaches the making of non-infections HIV-like particles comprising the viral envelope proteins. See, abstract and page 90, right column (teaching in the right column that the particles were produced from vectors encoding all of the viral genes except the nef gene, and that the result VLPs are "similar in structure to mature, infectious HIV virions"). The reference teaches the use of such particles for the study of infectious virions, and that the use has advantages over the use of live virions in that the particles are non-infectious, and that they may be safely produced in large quantities. Pages 89-90. From these teachings, it would have been obvious to those of ordinary skill in the art that these particles could also be used in the methods suggested by the Furata reference for determining the ability of stabilizing peptides to bind to sCD4 activated HIV envelope proteins. This is because it would have been clear to those of ordinary skill in the art that the cells of Furata and the particle of Haddrick are, for the purposes of detecting such binding, functional equivalents in that both present the envelope proteins for such binding.

Those in the art would have had a reasonable expectation of success in the use of the particles based on the teachings in the Haddrick reference that the VLP are useful for the study of the virus, and the indication that the particles are structurally similar to the mature infectious particles except that the lack the infectious RNA.

The combined teachings of these references therefore render the claimed inventions obvious.

Conclusion

27. No claims are allowed.

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 3/19/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600